

Prevalence and Correlates of Prescription Drug Misuse Among Spanish Adolescents

Sara Weidberg, Gema Aonso-Diego, Gloria García-Fernández, and Roberto Secades-Villa
Universidad de Oviedo

Abstract

Background: Prescription drug (PD) misuse among adolescents constitutes a growing health concern worldwide. This study aimed to provide up-to-date prevalence and correlates of PD misuse (i.e., tranquilizers, opioids and stimulants) among a national representative sample of high-school adolescents in Spain. **Method:** We used nationwide data from 36,788 adolescents (51.93% females) aged between 14 and 18 who completed the 2018-2019 Survey on Drug Use in Secondary Education in Spain (ESTUDES). Lifetime misuse of the following PD was assessed: tranquilizers without prescription, opioids to get high, and prescription stimulants to improve academic performance. Other substance use, sociodemographic characteristics, academic performance related variables, and the quality of parental relationship were assessed. **Results:** Lifetime prevalence of PD misuse was 8.50% for tranquilizers, 2.34% for stimulants, and 2.20% for opioids. Past-month tobacco use and lifetime illegal substance use were the only correlates associated with all PD categories (ORs between 1.419 and 6.788). The remaining sociodemographic, academic and family correlates were PD category-specific. **Conclusions:** This information may help in the development of empirically-based preventive interventions.

Keywords: Prescription drugs, misuse, adolescents, prevalence, correlates.

Resumen

Prevalencia y Correlatos del Consumo de Fármacos de Prescripción Entre Adolescentes Españoles. Antecedentes: el consumo de fármacos de prescripción (FP) en los adolescentes constituye un problema creciente. El objetivo de este estudio fue proporcionar una estimación de las prevalencias y correlatos de los FP (i.e., tranquilizantes, opioides y estimulantes) en una muestra representativa de adolescentes en España. **Método:** 36.788 adolescentes (51,93% mujeres) de edades comprendidas entre 14 y 18 años completaron la Encuesta 2018-2019 sobre uso de drogas en Enseñanzas Secundarias en España (ESTUDES). Se evaluó la prevalencia-vida de los siguientes FP: tranquilizantes sin prescripción, opioides para colocarse y estimulantes de prescripción para mejorar el rendimiento académico. También se evaluó el consumo de otras sustancias, las características sociodemográficas, variables académicas y las relaciones parentales. **Resultados:** la prevalencia-vida fue de 8,50% para tranquilizantes, 2,34% para estimulantes y 2,20% para opioides. El consumo de tabaco en el último mes y el consumo de sustancias ilegales alguna vez en la vida se asociaron con el uso de los tres FP (OR entre 1,419 y 6,788). El resto de las variables sociodemográficas, académicas y familiares estuvieron relacionadas con una categoría específica de FP. **Conclusiones:** esta información puede ser de ayuda en el desarrollo de intervenciones preventiva basadas en la evidencia. **Palabras clave:** fármacos de prescripción, uso indebido, adolescentes, prevalencia, correlatos.

Misuse of prescription drugs (PD) refers to the use of medication (including tranquilizers, opioids and prescription stimulants) without a corresponding medical prescription and in a manner other than normally prescribed, or in order to experience sensations the drug provides (Substance Abuse and Mental Health Services Administration [SAMHSA], 2015). PD misuse among adolescents is a growing public health concern worldwide, with 8.6% of US adolescents aged between 17 and 18 having taken some PD beyond medical use in 2019 (Miech et al., 2019). Likewise, lifetime prevalence of tranquilizer/sedative and painkiller misuse among European adolescents aged 15-16 was 6.6% and 4%, respectively,

with Spain showing estimates of 4% and 1.1% (European Monitoring Centre for Drugs and Drug Addiction, 2019a). Although there are few longitudinal studies conducted specifically among Spanish adolescents, previous research highlights the increasing trend in the prevalence of tranquilizer, sedative and sleeping-pill misuse, which has risen from 2.40% in 2004 to 2.96% in 2014 (Carrasco-Garrido et al., 2018). Seizures of PD have increased markedly since 2017 (European Monitoring Centre for Drugs and Drug Addiction, 2019b), suggesting that PD will play an increasing role in the European substance use scene in the near future.

The most concerning risks associated with PD misuse are both the acute health effects (overdose, death, and medical complications; Gomes et al., 2018), and the short and long-term adverse consequences, particularly in adolescence. These include poor academic performance (Arria et al., 2017), delinquency (Drazdowski et al., 2015), later PD dependence (McCabe et al., 2007), affective disorders (Becker et al., 2007; Grattan et al., 2012), sexual risk behaviors (Bonar et al., 2014) and suicidal ideation (Ford & Perna, 2015).

Previous research analyzing factors that may influence PD misuse among adolescent population has shown that PD misuse is associated with other substances use, both legal (Griffin et al., 2019; McCabe et al., 2017) and illegal (Carrasco-Garrido et al., 2018; McCabe & West, 2014), mainly with marijuana and alcohol (McCabe et al., 2020; Schepis et al., 2016). PD misuse also correlates with poor parental bonding (Cheng & Lo, 2012; Vaughn et al., 2012; Ward et al., 2018). The effect of age has also been proven, with older adolescents having increased odds of PD misuse than younger ones (Carmona et al., 2020; Young et al., 2012).

The association with other relevant sociodemographic variables remains unclear. Data shows that the percentage of adolescent girls misusing tranquilizers/sedatives is double that of adolescent boys (Carrasco-Garrido et al., 2019; Opaleye et al., 2014; Young et al., 2012). However, there are mixed results regarding the effect of gender on other PD categories. For instance, while some studies show that female adolescents have a higher likelihood of misusing opioids (Carmona et al., 2020; Rabinowitz et al., 2021) or stimulants (Striley et al., 2017) than male adolescents, others show the opposite pattern (Catalano et al., 2011; Hachtel & Armstrong, 2019; McCabe et al., 2020). The effect of the family socioeconomic status (SES) is also controversial, with some studies showing that adolescents living in families with lower SES are a particular at-risk sub-group for PD misuse (Fotiou et al., 2014; Sung et al., 2005), while others finding that young adults who grew up in higher socioeconomic environments are more likely to have ever engaged in PD misuse (Stewart & Reed, 2015).

The effect of immigrant status remains largely unexplored (Carrasco-Garrido, Jiménez-Trujillo et al., 2021), and mixed results have been obtained, with some studies highlighting its protective effect against PD misuse (Cristini et al., 2015), while others showing higher rates of PD misuse among immigrant adolescents (Carrasco-Garrido, Díaz Rodríguez et al., 2021). Finally, although school bonding appears to be negatively associated with PD misuse (see Nargiso et al., 2015 for a review), results on academic performance are unclear; while Collins et al. (2011) show no relationship between PD misuse and school grade, other research finds an inverse association between both variables (Arria et al., 2008).

Understanding the scope of PD misuse during adolescence is fundamental, since throughout this developmental period there are specific drug use patterns in which experimentation and peer pressure components are involved (Carrasco-Garrido et al., 2018), coupled with a perceived lack of risk of PD use (Netemeyer et al., 2015). Our study aims to extend prior investigations on PD misuse among adolescents by drawing on a large, nationally representative sample of Spain's adolescents, obtained from the Survey on Drug use in Secondary Education in Spain (ESTUDES; Plan Nacional sobre Drogas, 2020). The specific goals of the present study were to estimate the prevalence of lifetime PD misuse by PD category among adolescents (i.e., tranquilizers, opioids and stimulants), and to identify common and substance-specific correlates of PD misuse among this population.

Method

Participants

The study is based on data from the Survey on Drug Use in Secondary Education in Spain (ESTUDES; Plan Nacional sobre

Drogas, 2020), a representative survey of substance use in Spanish adolescents. The sampling was performed by two-stage conglomerates: 1) random selection of the educational centers, and 2) random selection of two classrooms from each selected center. In this way, all educational centers had the same probability of being selected.

The inclusion criteria were being between 14 and 18 years old, and being students enrolled in 3rd and 4th years of secondary education [level 3 of the International Standard Classification of Education (ISCED; UNESCO, 2011); upper secondary education], 1st and 2nd years of baccalaureate level [level 4 of the ISCED (UNESCO, 2011); post-secondary non-tertiary education], or 1st and 2nd years of basic and intermediate vocational training [level 5 of the ISCED (UNESCO, 2011); short-cycle tertiary education]. Thereby, if an 18-year-old student was pursuing university studies, such adolescent was not included in the study, as well as if a student did not attend class on the day of the survey.

A total of 38,010 adolescents responded to the survey, pertaining to 917 educational centers (68.4% public centers) and 1,769 classrooms. The final sample for this study was comprised of 36,788 participants ($M_{age} = 15.7$; $SD = 1.2$; 51.93% females), given that it included those adolescents who have ever used one PD (i.e., tranquilizers, opioids or stimulants), or who did not use any of these PD categories, in order to establish the comparison group. Thus, the participants were divided into four groups according to PD misuse: 1) a comparison group, which included participants who misused any substance, either legal or illegal, except for tranquilizers, opioids, or stimulants ($n = 33,640$); 2) lifetime tranquilizer misusers (but not opioids or stimulants; $n = 2,511$); 3) lifetime opioids misusers (but not tranquilizers or stimulants; $n = 421$); and 4) lifetime stimulant misusers (but not opioids or tranquilizers; $n = 216$).

Participants were enrolled in secondary education (55.8%, $n = 20,523$), baccalaureate (36.8%, $n = 13,553$), basic vocational training (3.8%, $n = 1,463$) and intermediate vocational training (7.4%, $n = 2,712$).

Instruments

The ESTUDES (Plan Nacional sobre Drogas, 2020) consists of an anonymous, self-reported, paper-and-pencil assessment survey, which collects data from addictive behaviors among adolescents between 14 and 18 years old.

Participants completed the standardized survey, which gathered data from sociodemographic characteristics (i.e., age, sex, nationality, and SES), academic performance related variables (i.e., skipping classes, grade point average, and repeating academic year), relationship with parents, and substance use. The nationality variable was dichotomized into having been born in Spain versus having been born abroad, with different countries merged in the last category. On the other hand, repeating academic year was dichotomized in a yes/no scale although the survey differentiated between having repeated a year or two. The reason for merging the categories was exclusively methodological, given the low sample size in the original categories.

Regarding the substance use variables, adolescents were asked about PD misuse. Specifically, they were questioned about the lifetime use of tranquilizers without prescription (i.e., sedative-hypnotics, benzodiazepines, or barbiturates), opioids to get high (i.e., fentanyl, morphine, tramadol, or codeine), and

prescription stimulants to improve their academic performance (i.e., methylphenidate, lisdexamfetamine, adderall, piracetam, donepezil, modafinil, or durvitan). Additionally, the survey included both legal (i.e., past-month tobacco and alcohol use), and illegal substance use. Specifically, it assessed past-month cannabis use, and lifetime use of cocaine, ecstasy, amphetamine, hallucinogens, heroin, volatile inhalants, GHB, methamphetamine, mushrooms, anabolic steroids, ketamine, spice, mephedrone, salvia, and ayahuasca. Further, data on having received information about either legal or illegal drugs was also collected.

Previous nationwide studies conducted with this large dataset support the suitability of the ESTUDES to conduct epidemiological research on substance use within the adolescent population in Spain (see e.g., Alarcó-Rosales et al., 2019; Belzunegui-Eraso et al., 2020).

Procedure

This study does not contain data from human participants collected by any of the authors. Given its epidemiological nature, it was exempted from the ethics committee approval of the Institutional Review Board of the University of Oviedo. When data were primarily collected, participants were informed that the survey was anonymous, and it did not include any personal information that would enable their identification. Participants were told that their responses would be treated combined with that of the remaining students, and no data would be obtained by specific classroom of educational center. The survey was completed during a regular class, which lasted between 45-60 minutes. Data collection took place between February and April 2019. The study was performed according to the stipulations of the Law 957/2020 (Boletín Oficial del Estado, 2021), and outside the assumptions established in the Article 2.e of the Law 14/2007 (Boletín Oficial del Estado, 2007) concerning biomedical research in Spain.

Data analysis

Descriptive and frequency analyses were conducted to examine participants' prevalence of each specific PD category, as well as substance use, sociodemographic, academic and family characteristics for each of the four aforementioned study groups. Differences between groups were carried out using analysis of variance (ANOVA) for continuous variables and chi-square for categorical ones. Effect size estimates were calculated using Cohen's *d*, and Cramer's *V*, as appropriate.

A multinomial logistic regression analysis was performed with the aforementioned study groups (i.e., comparison group, tranquilizer misusers, opioid analgesics misusers, and prescription stimulants misusers) as the dependent variable, using the comparison group as a reference category. The independent variables introduced were: 1) sociodemographics: age, sex, nationality, and self-reported SES (below average, average, above average); 2) academic performance: skipping classes (dichotomized), repeating academic year (dichotomized), and grade point average (below 4, 5-6, or more than 7, on a 10-point scale); relationship with the parents: perceived relationship with their mother and with their father (good and very good relationship, intermediate relationship, and bad or very bad relationship); and 4) substance use: past-month tobacco, alcohol and cannabis use, and lifetime illegal

substance use (other than cannabis and any kind of PD), all of them dichotomized on a yes/no scale. All analyses were carried out using statistical package SPSS (V24; SPSS, Inc., Chicago, IL).

Results

Prevalence of prescription drug misuse

Lifetime misuse of any PD categories were 9.78% ($n = 3,718$). The most prevalent PD misused are tranquilizers (sedative, hypnotics, benzodiazepines, and barbiturates). Specifically, a total of 8.50% of the adolescents assessed ($n = 3,231$) have ever misused them, 6.01% ($n = 2,291$) in the past year, and 2.88% ($n = 1,094$) in the past month. On average, misuse onset occurred when adolescents had 14.3 years old ($SD = 2.1$).

With regard to opioids, 2.20% of adolescents ($n = 837$) reported to have ever misused them to get high, 1.46% in the past year ($n = 554$), and 0.46% in the past month ($n = 174$). Mean age of consumptions onset was 15.1 years old ($SD = 1.9$).

Finally, a total of 2.34% of adolescents ($n = 889$) have ever misused prescription stimulants to improve their academic performance. Among those who reported their misuse, the prevalence according to the specific stimulant were the following: methylphenidate (35.43%, $n = 315$), piracetam (18.22%, $n = 162$), lisdexamfetamine or adderall (16.31%, $n = 145$), donepezil (10.57%, $n = 94$), durvitan (10.01%, $n = 89$), and modafinil (9.44%, $n = 84$).

Substance use, sociodemographics, academic and family characteristics of each of the four groups (i.e., comparison group, tranquilizer misusers, opioids misusers, and stimulants misusers) are shown in Table 1.

Correlates of prescription drugs misuse

Results of multinomial regression analyses are displayed in Table 2. Findings indicated that tobacco use and illegal substance use were common correlates across all categories of PD misuse (*OR* between 1.419 and 2.238 and *OR* between 2.071 and 6.788, respectively). Past-month alcohol and cannabis use was associated to tranquilizers (*OR* = 1.391 and *OR* = 1.238, respectively) and opioids misuse (*OR* = 1.871 and *OR* = 2.642, respectively).

With regard to sociodemographic characteristics, being older was related to lifetime tranquilizers (*OR* = 1.104) and stimulants misuse (*OR* = 1.249). Being female was related to tranquilizers use (*OR* = 1.712), while being male was associated with opioids use (*OR* = 2.188). Being born in a country other than Spain increased the odds of misusing opioid analgesics (*OR* = 1.574). Finally, having an above-average SES was related to tranquilizers misuse (*OR* = 1.176).

Concerning academic performance variables, skipping classes was significantly associated with tranquilizers (*OR* = 1.293) and opioids misuse (*OR* = 1.362). A grade point average lower than 4 (*OR* = 1.726) or between 5 and 6 (*OR* = 1.589) on a 10-point scale were significantly associated with stimulants misuse.

Having an intermediate quality relationship with both their mother and father (*OR* = 1.210, and *OR* = 1.424, respectively) or a bad relationship with their father (*OR* = 1.382), were also associated with tranquilizers misuse. Further, having an intermediate quality relationship with their mother (*OR* = 1.642) was associated with stimulants misuse.

Table 1
Characteristics of groups based on prescription drug misuse.

	Comparison group (n = 33640)	Tranquilizers (n = 2511)	Opioid analgesics (n = 421)	Prescription stimulants (n = 216)
Sociodemographic characteristics				
Age ^a	15.7 (1.2)	15.9 (1.2)	16 (1.1)	16 (1.3)
Gender (female)	17,236 (51.23%)	1,629 (64.87%)	141 (33.49%)	99 (45.83%)
Nationality (Spanish)	30,518 (90.72%)	2,253 (89.72%)	366 (86.93%)	199 (92.13%)
SES				
Below average	4,383 (13.03%)	374 (14.89%)	71 (16.86%)	39 (18.05%)
Average	1,270 (3.77%)	147 (5.85%)	26 (6.17%)	11 (5.09%)
Above average	27,589 (82.01%)	1,970 (78.45%)	321 (76.24%)	162 (75%)
Academic performance				
Skip classes	7139 (21.22%)	873 (34.76%)	208 (49.41%)	82 (37.96%)
Repeat academic year	7,295 (31.68%)	670 (26.68%)	167 (39.66%)	83 (38.42%)
Grade point average (0-10)				
Fail (0-4)	2,163 (6.43%)	201 (8.01%)	54 (12.82%)	35 (16.20%)
Pass (5-6)	15,701 (46.67%)	1,249 (49.74%)	239 (56.77%)	121 (56.01%)
Good (+7)	15,651 (46.52%)	1,052 (41.89%)	128 (30.40%)	58 (26.85%)
Relationship with mother				
Good or very good	28,363 (84.31%)	1,912 (76.14%)	310 (73.63%)	149 (68.98%)
Intermediate	3,908 (11.61%)	426 (16.96%)	78 (18.52%)	40 (18.51%)
Bad or very bad	598 (1.77%)	97 (3.86%)	19 (4.51%)	10 (4.63%)
Relationship with father				
Good or very good	25,203 (74.92%)	1,534 (61.09%)	264 (62.71%)	140 (64.81%)
Intermediate	5,518 (16.40%)	607 (24.17%)	92 (21.85%)	40 (18.51%)
Bad or very bad	1,204 (3.58%)	185 (7.36%)	29 (6.88%)	12 (5.55%)
Substance use related variables				
Past-month tobacco use	3,998 (11.88%)	912 (36.32%)	271 (64.37%)	92 (42.59%)
Past-month alcohol use	15,897 (47.25%)	1,541 (61.37%)	344 (81.71%)	121 (56.02%)
Past-month cannabis use	3,874 (11.51%)	561 (22.34%)	234 (55.58%)	60 (27.77%)
Lifetime illegal substance use ^b	1,105 (3.28%)	270 (10.75%)	169 (40.14%)	39 (18.05%)
Information about legal and illegal substances	27,652 (82.19%)	2,069 (82.39%)	343 (81.47%)	167 (77.31%)

Note: ^aMean (standard deviation); ^bIncluding cocaine, ecstasy, amphetamine, hallucinogens, heroin, volatile inhalants, GHB, methamphetamine, mushrooms, anabolic steroids, ketamine, spice, mephredrone, salvia, and ayahuasca; SES = socioeconomic status

Discussion

In a large, nationally representative sample of Spanish adolescents, the lifetime prevalence of PD misuse was highest for tranquilizers (8.50%), followed by stimulants (2.34%) and lastly opioids (2.20%). Past-month tobacco use and lifetime illegal substance use were common correlates across all PD categories. Past-month alcohol and cannabis use, as well as the remaining sociodemographic, academic and family correlates were specific for certain PD categories.

Consistent with previous research (Griffin et al., 2019; Kelly et al., 2014; Novak et al., 2016), illegal substance use (other than cannabis) as well as tobacco use were the only two correlates associated with all PD categories, with the highest ORs observed for opioid analgesics. This finding indicates that PD misuse among adolescents does not occur isolated, but instead those misusing PD may be adding them to a variety of other substances (Catalano et al., 2011), which may result in enhanced reinforcement (Compton & Volkow, 2006). The combination of PD with other substances, especially the illicit ones, usually occurs in nightlife contexts (Kelly et al., 2014), which suggests that motives and contexts for co-use are mainly social and recreational in nature (McCabe et al., 2015). In these contexts, PD misuse may serve as a way to compensate for or potentiate the effects of other substances or wanting to experience new sensations (Carrasco-Garrido et al., 2018).

Certain correlates were associated with specific PD categories. Adolescents who use cannabis and alcohol were more likely to misuse tranquilizers and opioids, a finding that is similar to previous evidence (Hudgins et al., 2019; McCabe et al., 2020; Schepis et al., 2016). These substances share similar pharmacological and neuropsychological effects such as analgesia, sedation or reduced attention (Serrano & Parsons, 2011; Winward et al., 2014). Preclinical research has also proven the existence of related neurochemical mechanisms for cannabinoids and opioids (Abrams et al., 2011) as well as for tranquilizers and alcohol (Krystal et al., 2006). These linked neural pathways are responsible for cross-tolerance and synergistic effects observed when co-using these substances, thus increasing their abuse liability (McCabe et al., 2012; Nattala et al., 2012). Such between-substance synergistic interactions may also lead to higher perceived benefits compared to their isolated use, such as increased drug reward or enhanced pain relief (McCabe et al., 2012).

In accordance with previous studies (Carrasco-Garrido et al., 2018; Opaleye et al., 2014), females were more likely to misuse tranquilizers than males and, conversely, males were more likely to misuse opioids than females (Catalano et al., 2011; McCabe et al., 2020). The higher prevalence of stress and anxiety related problems among female adolescents (Bahrami & Yousefi, 2011; Fernández-Artamendi et al., 2021; Landstedt & Gådin, 2012) may

Table 2
Predictors of prescription drug misuse

	Tranquilizers			Opioid analgesics			Prescription stimulants		
	B	OR [95%CI]	p	B	OR [95%CI]	p	B	OR [95%CI]	p
Sociodemographic characteristics									
Age	.099	1.104 [1.050, 1.161]	<.001	-.047	.954 [.746, 1.076]	.446	.222	1.249 [1.052, 1.482]	.011
Gender (female)	.537	1.712 [1.525, 1.921]	<.001	-.783	.457 [.347, .601]	<.001	.115	1.121 [.772, 1.629]	.548
Nationality (Spanish)	.047	1.048 [.858, 1.281]	.643	-.454	.635 [.425, .948]	.026	.391	1.479 [.712, 3.072]	.294
SES									
Below average (vs. average)	.191	1.210 [.942, 1.555]	.136	-.001	.999 [.558, 1.787]	.996	-.091	.913 [.365, 2.286]	.847
Above average (vs. average)	.162	1.176 [1.007, 1.373]	.041	-.073	.929 [.657, 1.314]	.678	.448	1.565 [.972, 2.519]	.065
Academic performance									
Skip classes	.257	1.293 [1.140, 1.467]	<.001	.309	1.363 [1.033, 1.797]	.029	.084	1.087 [.709, 1.668]	.701
Repeat academic year	-.003	.997 [.865, 1.150]	.969	.131	1.140 [.850, 1.528]	.382	.142	1.152 [.743, 1.787]	.526
Grade point average (0-10)									
Fail (0-4) (vs. pass)	-.160	.852 [.680, 1.067]	.163	-.182	.833 [.550, 1.262]	.389	-.5456	1.726 [1.005, 2.964]	.048
Good (+7) (vs. pass)	.003	1.003 [.893, 1.128]	.954	.133	1.142 [.856, 1.525]	.366	-.464	.629 [.409, .967]	.035
Relationship with mother									
Good or very good (vs. intermediate)	-.187	.829 [.710, .968]	.018	-.185	.831 [.586, 1.180]	.302	-.495	.609 [.372, .997]	.049
Bad or very bad (vs. intermediate)	.088	1.092 [.786, 1.519]	.599	-.206	.814 [.407, 1.625]	.559	-.584	.558 [.163, 1.910]	.353
Relationship with father									
Good or very good (vs. intermediate)	-.354	.702 [.612, .804]	<.001	-.121	.886 [.640, 1.229]	.469	.128	1.137 [.690, 1.872]	.614
Bad or very bad (vs. intermediate)	.324	1.382 [1.103, 1.732]	.005	.494	1.639 [.980, 2.742]	.060	.589	1.801 [.818, 3.967]	.144
Substance use related variables									
Past-month tobacco use	.350	1.419 [1.228, 1.640]	<.001	.805	2.238 [1.565, 3.200]	<.001	.614	1.847 [1.121, 3.043]	.016
Past-month alcohol use	.330	1.391 [1.221, 1.583]	<.001	.627	1.871 [1.248, 2.807]	.002	-.233	.792 [.505, 1.241]	.309
Past-month cannabis use	.214	1.238 [1.054, 1.455]	.009	.972	2.642 [1.871, 3.732]	<.001	.040	1.041 [.611, 1.772]	.882
Lifetime illegal substance use ^a	.728	2.071 [1.711, 2.507]	<.001	1.915	6.788 [5.094, 9.046]	<.001	1.258	3.518 [2.080, 5.949]	<.001
Information about legal and illegal substances	-.038	.962 [.830, 1.116]	.613	.081	1.085 [.785, 1.498]	.621	-.225	.798 [.475, 1.342]	.395

Note: ^aIncluding cocaine, ecstasy, amphetamine, hallucinogens, heroin, volatile inhalants, GHB, methamphetamine, mushrooms, anabolic steroids, ketamine, spice, mephedrone, salvia, and ayahuasca; OR = odds ratio; SES = socioeconomic status

account for the misuse of tranquilizers as a mean of self-medicating. Conversely, the leading source of obtaining opioid analgesics are friends (McCabe et al., 2007), and the fact that male adolescents are more likely to engage in peer-to-peer diversion of opioids (that is, sharing, trading or selling) with friends than female adolescents (McCabe et al., 2007) may explain the higher prevalence of this specific PD among male adolescents.

Higher SES was associated with tranquilizers misuse, a finding that aligns with prior research (Stewart & Reed, 2015). Adolescents who come from wealthier families may have increased financial resources to buy tranquilizers and/or higher access to social relationships with others with high SES that could obtain them (Janicijevic et al., 2017). Also, the experience of more pressure to achieve combined with isolation of parents who have more demanding careers or jobs (Janicijevic et al., 2017), could explain this result.

We found that skipping classes was associated with both tranquilizers and opioids misuse, while low grade point average was associated with stimulants misuse, even when students were asked if they misused these substances to improve their academic performance. This finding aligns with prior evidence showing that increases in skipping classes are associated with a range of substance use problems, starting from alcohol and cannabis use disorders and escalating to PD misuse (Arria et al., 2008, 2013), and that the use of prescription stimulants for study purposes was, in fact, associated with academic difficulties and lower grade point average among college students (Arria et al., 2013).

Finally, adolescents' relationship with their parents was associated with both tranquilizers and stimulants misuse, which is consistent with prior research (Nargiso et al., 2015). A weak parental bonding may increase PD misuse because adolescents believe that their potential deviant behavior is not going to be detected and punished. Also, weak parental bonding is associated with less time spent with parents, thus increasing the chances of peer socializing in an unstructured setting where tranquilizers and prescription stimulants may be present (Ford, 2009).

The present study is subject to several limitations common to most large-scale surveys. First, information on substance use was based on self-report and not confirmed by objective methods. Second, some methodological limitations (i.e., the cross-sectional inherent design of the ESTUDES survey and the unbalanced number of participants included in each of the study groups) limit the results found. Nevertheless, such sample unbalance is compensated by a high sample size per group, even in the PD category with the least prevalence of misuse (i.e., opioids). Third, data on each PD category was collected jointly, so it is not possible to determine which specific PD is used within each PD category (e.g., data collection prevents knowing whether a given participant that reported tranquilizers misuse, consumes benzodiazepines or barbiturates). Fourth, the ESTUDES survey excluded non-scholarized adolescents, which may have changed the probability of having a history of PD misuse. Lastly, relevant variables such as PD accessibility, availability, or the specific sources used to

obtain PD (e.g., parents, siblings, peers...) were not assessed. Strengths of this study include the use of a representative national sample and the control of a wide range of correlates from different domains.

Despite the aforementioned shortcomings, the present study indicates that lifetime prevalence of PD misuse was highest for tranquilizers, followed by stimulants and opioids. Past-month tobacco use and lifetime illegal substance use were common correlates across all PD categories, whereas the remaining correlates were specific for certain PD categories. These findings

emphasize the importance of developing effective intervention strategies directed at curtailing PD in this population. Approaches that include education on the health risks of PD misuse, skills training to deal with peer pressure and anxiety (especially among female adolescents, who show higher prevalence of tranquilizers misuse) and parental competences on how to improve family relationships are highly encouraged (Perlmutter et al., 2018). These results also highlight the need for controlling and restricting the illicit market of PD and the medical prescription and supplies of PD by healthcare professionals.

References

- Abrams, D. I., Couey, P., Shade, S. B., Kelly, M. E., & Benowitz, N. L. (2011). Cannabinoid-opioid interaction in chronic pain. *Clinical Pharmacology and Therapeutics*, *90*(6), 844-851. <https://doi.org/10.1038/clpt.2011.188>
- Alarcó-Rosales, R., Sánchez-SanSegundo, M., Ferrer-Cascales, R., Albaladejo-Blázquez, N., Ruiz-Robledillo, N., Delvecchio, E., & Oltra-Cucarella, J. (2019). Relationships between problematic cannabis use and risky behaviors in Spanish adolescents. *International Journal of Environmental Research and Public Health*, *16*(17), 3029. <https://doi.org/10.3390/ijerph16173029>
- Arria, A. M., Caldeira, K. M., Vincent, K. B., O'Grady, K. E., Cimini, M. D., Geisner, I. M., Fossos-Wong, N., Kilmer, J. R., & Larimer, M. E. (2017). Do college students improve their grades by using prescription stimulants nonmedically? *Addictive Behaviors*, *65*, 245-249. <https://doi.org/10.1016/j.addbeh.2016.07.016>
- Arria, A. M., O'Grady, K. E., Caldeira, K. M., Vincent, K. B., & Wish, E. D. (2008). Nonmedical use of prescription stimulants and analgesics: Associations with social and academic behaviors among college students. *Journal of Drug Issues*, *38*(4), 1045-1060. <https://doi.org/10.1177/002204260803800406>
- Arria, A. M., Wilcox, H. C., Caldeira, K. M., Vincent, K. B., Garnier-Dykstra, L. M., & O'Grady, K. E. (2013). Dispelling the myth of "smart drugs": Cannabis and alcohol use problems predict nonmedical use of prescription stimulants for studying. *Addictive Behaviors*, *38*(3), 1643-1650. <https://doi.org/10.1016/j.addbeh.2012.10.002>
- Bahrami, F., & Yousefi, N. (2011). Females are more anxious than males: A metacognitive perspective. *Iranian Journal of Psychiatry and Behavioral Sciences*, *5*(2), 83-90. <https://doi.org/www.ncbi.nlm.nih.gov/pmc/articles/PMC3939970/pdf/ijpbs-005-083.pdf>
- Becker, W. C., Fiellin, D. A., & Desai, R. A. (2007). Non-medical use, abuse and dependence on sedatives and tranquilizers among U.S. adults: Psychiatric and socio-demographic correlates. *Drug and Alcohol Dependence*, *90*(2-3), 280-287. <https://doi.org/10.1016/j.drugalcdep.2007.04.009>
- Belzunegui-Eraso, A., Pastor-Gosálbez, I., Raigal-Aran, L., Valls-Fonayet, F., Fernández-Aliseda, S., & Torres-Coronas, T. (2020). Substance use among Spanish adolescents: The information Paradox. *International Journal of Environmental Research and Public Health*, *17*(2), Article 627. <https://doi.org/10.3390/ijerph17020627>
- Boletín Oficial del Estado (2007). *Ley 14/2007 de investigación biomédica* [Law 14/2007 on biomedical research]. <https://www.boe.es/boe/dias/2007/07/04/pdfs/A28826-28848.pdf>
- Boletín Oficial del Estado (2021). *Real Decreto 957/2020 por el que se regulan los estudios observacionales con medicamentos de uso humano* [Law 957/2020 on guidelines for observational studies in medical human research]. <https://www.boe.es/boe/dias/2007/07/04/pdfs/A28826-28848.pdf>
- Bonar, E. E., Cunningham, R. M., Chermack, S. T., Blow, F. C., Barry, K. L., Booth, B. M., & Walton, M. A. (2014). Prescription drug misuse and sexual risk behaviors among adolescents and emerging adults. *Journal of Studies on Alcohol and Drugs*, *75*(2), 259-268. <https://doi.org/10.15288/jsad.2014.75.259>
- Carmona, J., Maxwell, J. C., Park, J. Y., & Wu, L. T. (2020). Prevalence and Health Characteristics of Prescription Opioid Use, Misuse, and Use Disorders Among U.S. Adolescents. *Journal of Adolescent Health*, *66*(5), 536-544. <https://doi.org/10.1016/j.jadohealth.2019.11.306>
- Carrasco-Garrido, P., Díaz Rodríguez, D., Jiménez-Trujillo, I., Hernández-Barrera, V., Lima Florencio, L., & Palacios-Ceña, D. (2021). Nonmedical Use of Benzodiazepines among Immigrant and Native-Born Adolescents in Spain: National Trends and Related Factors. *International Journal of Environmental Research and Public Health*, *18*(3), 1-8. <https://doi.org/10.3390/IJERPH18031171>
- Carrasco-Garrido, P., Jiménez-Trujillo, I., Hernández-Barrera, V., Alonso-Fernández, N., García-Gómez-Heras, S., & Palacios-Ceña, D. (2019). Gender differences in the nonmedical use of psychoactive medications in the school population-national trends and related factors. *BMC Pediatrics*, *19*(1), 1-9. <https://doi.org/10.1186/s12887-019-1728-8>
- Carrasco-Garrido, P., Jiménez-Trujillo, I., Hernández-Barrera, V., García-Gómez-Heras, S., Alonso-Fernández, N., & Palacios-Ceña, D. (2018). Trends in the misuse of tranquilizers, sedatives, and sleeping pills by adolescents in Spain, 2004-2014. *Journal of Adolescent Health*, *63*(6), 709-716. <https://doi.org/10.1016/j.jadohealth.2018.04.003>
- Carrasco-Garrido, P., Jiménez-Trujillo, I., Hernández-Barrera, V., Lima Florencio, L., & Palacios-Ceña, D. (2021). Patterns of non-medical use of benzodiazepines and Z-Drugs among adolescents and young adults: Gender differences and related factors. *Journal of Substance Use*, *26*(2), 190-196. <https://doi.org/10.1080/14659891.2020.1800846>
- Catalano, R. F., White, H. R., Fleming, C. B., & Haggerty, K. P. (2011). Is nonmedical prescription opiate use a unique form of illicit drug use? *Addictive Behaviors*, *36*(1-2), 79-86. <https://doi.org/10.1016/j.addbeh.2010.08.028>
- Cheng, T. C., & Lo, C. C. (2012). Nonmedical use of prescription medications: A longitudinal analysis with adolescents involved in child welfare. *Children and Youth Services Review*, *34*(4), 859-864. <https://doi.org/10.1016/j.childyouth.2012.01.021>
- Collins, D., Abadi, M. H., Johnson, K., Shamblen, S., & Thompson, K. (2011). Non-medical use of prescription drugs among youth in an appalachian population: Prevalence, predictors, and implications for prevention. *Journal of Drug Education*, *41*(3), 309-326. <https://doi.org/10.2190/DE.41.3.e>
- Compton, W. M., & Volkow, N. D. (2006). Abuse of prescription drugs and the risk of addiction. *Drug and Alcohol Dependence*, *83*, S4-S7. <https://doi.org/10.1016/j.drugalcdep.2005.10.020>
- Cristini, F., Scacchi, L., Perkins, D. D., Bless, K. D., & Vieno, A. (2015). Drug Use Among Immigrant and Non-immigrant Adolescents: Immigrant Paradox, Family and Peer Influences. *Journal of Community & Applied Social Psychology*, *25*(6), 531-548. <https://doi.org/10.1002/CASP.2232>
- Drazdowski, T. K., Jäggi, L., Borre, A., & Kliever, W. L. (2015). Use of prescription drugs and future delinquency among adolescent offenders. *Journal of Substance Abuse Treatment*, *48*(1), 28-36. <https://doi.org/10.1016/j.jsat.2014.07.008>
- European Monitoring Centre for Drugs and Drug Addiction (2019a). *ESPAD Report 2019 Results from the European School Survey Project on Alcohol and Other Drugs*. http://www.espad.org/sites/espad.%0Aorg/files/ESPAD_report_2019.pdf

- European Monitoring Centre for Drugs and Drug Addiction (2019b). *European drug use report 2019*. https://www.emcdda.europa.eu/publications/edr/trends-developments/2019_en
- Fernández-Artamendi, S., Martínez-Loredo, V., & López-Núñez, C. (2021). Sex Differences in Comorbidity Between Substance Use and Mental Health in Adolescents: Two Sides of the Same Coin. *Psicothema*, *33*(1), 36-43. <https://doi.org/10.7334/PSICOTHEMA2020.297>
- Ford, J. A. (2009). Nonmedical prescription drug use among adolescents: The influence of bonds to family and school. *Youth and Society*, *40*(3), 336-352. <https://doi.org/10.1177/0044118X08316345>
- Ford, J. A., & Perna, D. (2015). Prescription drug misuse and suicidal ideation: Findings from the National Survey on Drug Use and Health. *Drug and Alcohol Dependence*, *157*, 192-196. <https://doi.org/10.1016/j.drugalcdep.2015.10.010>
- Fotiou, A., Kanavou, E., Richardson, C., Ploumpidis, D., & Kokkevi, A. (2014). Misuse of prescription opioid analgesics among adolescents in Greece: The importance of peer use and past prescriptions. *Drugs: Education, Prevention and Policy*, *21*(5), 357-369. <https://doi.org/10.3109/09687637.2014.899989>
- Gomes, T., Tadrous, M., Mamdani, M. M., Paterson, J. M., & Juurlink, D. N. (2018). The Burden of Opioid-Related Mortality in the United States. *JAMA Network Open*, *1*(2), e180217. <https://doi.org/10.1001/jamanetworkopen.2018.0217>
- Grattan, A., Sullivan, M. D., Saunders, K. W., Campbell, C. I., & von Korff, M. R. (2012). Depression and prescription opioid misuse among chronic opioid therapy recipients with no history of substance abuse. *Annals of Family Medicine*, *10*(4), 304-311. <https://doi.org/10.1370/afm.1371>
- Griffin, K. W., Lowe, S. R., Botvin, C., & Acevedo, B. P. (2019). Patterns of adolescent tobacco and alcohol use as predictors of illicit and prescription drug abuse in minority young adults. *Journal of Prevention and Intervention in the Community*, *47*(3), 228-242. <https://doi.org/10.1080/10852352.2019.1603672>
- Hachtel, J. C., & Armstrong, K. J. (2019). Illicit Use of Prescription Stimulants: Gender Differences in Perceptions of Risk. *Substance Use and Misuse*, *54*(10), 1654-1662. <https://doi.org/10.1080/10826084.2019.1608246>
- Hudgins, J. D., Porter, J. J., Monuteaux, M. C., & Bourgeois, F. T. (2019). Prescription opioid use and misuse among adolescents and young adults in the United States: A national survey study. *PLoS Medicine*, *16*(11), e1002922. <https://doi.org/10.1371/journal.pmed.1002922>
- Janicijevic, K. M., Kocic, S. S., Radevic, S. R., Jovanovic, M. R., & Radovanovic, S. M. (2017). Socioeconomic factors associated with psychoactive substance abuse by adolescents in Serbia. *Frontiers in Pharmacology*, *8*, Article 366. <https://doi.org/10.3389/fphar.2017.00366>
- Kelly, B. C., Wells, B. E., Pawson, M., LeClair, A., & Parsons, J. T. (2014). Combinations of prescription drug misuse and illicit drugs among young adults. *Addictive Behaviors*, *39*(5), 941-944. <https://doi.org/10.1016/j.addbeh.2013.12.003>
- Krystal, J. H., Staley, J., Mason, G., Petrakis, I. L., Kaufman, J., Harris, R. A., Gelernter, J., & Lappalainen, J. (2006). γ -Aminobutyric acid type A receptors and alcoholism: Intoxication, dependence, vulnerability, and treatment. *Archives of General Psychiatry*, *63*(9), 957-968. <https://doi.org/10.1001/archpsyc.63.9.957>
- Landstedt, E., & Gädin, K. G. (2012). Seventeen and stressed - Do gender and class matter? In *Health Sociology Review* (Vol. 21, Issue 1, pp. 82-98). Routledge. <https://doi.org/10.5172/hesr.2012.21.1.82>
- McCabe, S. E., Cranford, J. A., Boyd, C. J., & Teter, C. J. (2007). Motives, diversion and routes of administration associated with nonmedical use of prescription opioids. *Addictive Behaviors*, *32*(3), 562-575. <https://doi.org/10.1016/j.addbeh.2006.05.022>
- McCabe, S. E., Schulenberg, J., McCabe, V. V., & Veliz, P. T. (2020). Medical use and misuse of prescription opioids in US 12th-Grade youth: School-Level correlates. *Pediatrics*, *146*(4), e20200387. <https://doi.org/10.1542/peds.2020-022798>
- McCabe, S. E., Veliz, P., & Patrick, M. E. (2017). High-intensity drinking and nonmedical use of prescription drugs: Results from a national survey of 12th grade students. *Drug and Alcohol Dependence*, *178*, 372-379. <https://doi.org/10.1016/j.drugalcdep.2017.05.038>
- McCabe, S. E., & West, B. T. (2014). Medical and nonmedical use of prescription benzodiazepine anxiolytics among U.S. high school seniors. *Addictive Behaviors*, *39*(5), 959-964. <https://doi.org/10.1016/j.addbeh.2014.01.009>
- McCabe, S. E., West, B. T., Morales, M., Cranford, J. A., & Carol, J. (2007). Does early onset of non-medical use of prescription drugs predict subsequent prescription drug abuse and dependence? Results from a national study. *Addiction*, *102*(12), 1920-1930. <https://doi.org/10.1111/j.1360-0443.2007.02015.x>
- McCabe, S. E., West, B. T., Schepis, T. S., & Teter, C. J. (2015). Simultaneous co-ingestion of prescription stimulants, alcohol and other drugs: A multi-cohort national study of US adolescents. *Human Psychopharmacology*, *30*(1), 42-51. <https://doi.org/10.1002/hup.2449>
- McCabe, S. E., West, B. T., Teter, C. J., & Boyd, C. J. (2012). Co-ingestion of prescription opioids and other drugs among high school seniors: Results from a national study. *Drug and Alcohol Dependence*, *126*(1-2), 65-70. <https://doi.org/10.1016/j.drugalcdep.2012.04.017>
- Miech, R. A., Schulenberg, J. E., & Johnston, L. D., Bachman, J. G., O'Malley, P. M., & Patrick, M. E. (2019). *National Adolescent Drug Trends in 2019: Findings Released*. Monitoring the Future. <https://isr.umich.edu/news-events/news-releases/national-adolescent-drug-trends-in-2019-findings-released/>
- Nargiso, J. E., Ballard, E. L., & Skeer, M. R. (2015). A systematic review of risk and protective factors associated with nonmedical use of prescription drugs among youth in the United States: A social ecological perspective. *Journal of Studies on Alcohol and Drugs*, *76*(1), 5-20. <https://doi.org/10.15288/jsad.2015.76.5>
- Nattala, P., Leung, K. S., Abdallah, A. Ben, Murthy, P., & Cottler, L. B. (2012). Motives and simultaneous sedative-alcohol use among past 12-month alcohol and nonmedical sedative users. *American Journal of Drug and Alcohol Abuse*, *38*(4), 359-364. <https://doi.org/10.3109/00952990.2011.643987>
- Netemeyer, R., Burton, S., Delaney, B., & Hijjawi, G. (2015). The legal high: Factors affecting young consumers' risk perceptions and abuse of prescription drugs. *Journal of Public Policy and Marketing*, *34*(1), 103-118. <https://doi.org/10.1509/jppm.14.073>
- Novak, S. P., Håkansson, A., Martínez-Raga, J., Reimer, J., Krotki, K., & Varughese, S. (2016). Nonmedical use of prescription drugs in the European Union. *BMC Psychiatry*, *16*(1), 1-12. <https://doi.org/10.1186/s12888-016-0909-3>
- Opaleye, E. S., Ferri, C. P., Locatelli, D. P., Amato, T. C., & Noto, A. R. (2014). Nonprescribed use of tranquilizers and use of other drugs among Brazilian students. *Revista Brasileira de Psiquiatria*, *36*(1), 16-23. <https://doi.org/10.1590/1516-4446-2013-1180>
- Perlmuter, A., Bauman, M., Mantha, S., Segura, L., Ghandour, L., & Martins, S. (2018). Nonmedical Prescription Drug Use among Adolescents: Global Epidemiological Evidence for Prevention, Assessment, Diagnosis, and Treatment. *Current Addiction Reports*, *5*(2), 120-127. <https://doi.org/10.1007/s40429-018-0194-y>
- Plan Nacional sobre Drogas (2020). *INFORME 2020 Alcohol, tabaco y drogas ilegales en España. Encuesta sobre uso de drogas en Enseñanzas Secundarias en España (ESTUDES), 1994-2018/2019* [2020 Report on Alcohol, tobacco and illegal drugs in Spain. Survey on Drug Use in Secondary Education in Spain (ESTUDES), 1994-2018/2019]. <https://pnsd.sanidad.gob.es/>
- Rabinowitz, J. A., Reboussin, B. A., Thrul, J., Drabick, D. A. G., Kahn, G., Green, K. M., Ialongo, N. S., Huhn, A. S., & Maher, B. S. (2021). Early Childhood Behavioral and Academic Antecedents of Lifetime Opioid Misuse among Urban Youth. *Journal of Clinical Child and Adolescent Psychology*, *53*, 1-13. <https://doi.org/10.1080/15374416.2021.1875324>
- Schepis, T. S., West, B. T., Teter, C. J., & McCabe, S. E. (2016). Prevalence and correlates of co-ingestion of prescription tranquilizers and other psychoactive substances by U.S. high school seniors: Results from a national survey. *Addictive Behaviors*, *52*, 8-12. <https://doi.org/10.1016/j.addbeh.2015.08.002>
- Serrano, A., & Parsons, L. H. (2011). Endocannabinoid influence in drug reinforcement, dependence and addiction-related behaviors. *Pharmacology and Therapeutics*, *132*(3), 215-241. <https://doi.org/10.1016/j.pharmthera.2011.06.005>
- Stewart, T. D., & Reed, M. B. (2015). Lifetime nonmedical use of prescription medications and socioeconomic status among young adults in the United States. *American Journal of Drug and Alcohol Abuse*, *41*(5), 458-464. <https://doi.org/10.3109/00952990.2015.1060242>

- Striley, C. W., Kelso-Chichetto, N. E., & Cottler, L. B. (2017). Nonmedical Prescription Stimulant Use Among Girls 10-18 Years of Age: Associations With Other Risky Behavior. *Journal of Adolescent Health, 60*(3), 328-332. <https://doi.org/10.1016/j.jadohealth.2016.10.013>
- Substance Abuse and Mental Health Administration (2015). *Prescription Drug Use and Misuse in the United States: Results from the 2015 National Survey on Drug Use and Health*. <https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR2-2015/NSDUH-FFR2-2015.htm>
- Sung, H. E., Richter, L., Vaughan, R., Johnson, P. B., & Thom, B. (2005). Nonmedical use of prescription opioids among teenagers in the United States: Trends and correlates. *Journal of Adolescent Health, 37*(1), 44-51. <https://doi.org/10.1016/j.jadohealth.2005.02.013>
- UNESCO (2011). International Standard Classification of Education (ISCED). [https://ec.europa.eu/eurostat/statistics-explained/index.php?title=International_Standard_Classification_of_Education_\(ISCED\)#Correspondence_between_ISCED_2011_and_ISCED_1997](https://ec.europa.eu/eurostat/statistics-explained/index.php?title=International_Standard_Classification_of_Education_(ISCED)#Correspondence_between_ISCED_2011_and_ISCED_1997)
- Vaughn, M. G., Fu, Q., Perron, B. E., & Wu, L. T. (2012). Risk profiles among adolescent nonmedical opioid users in the United States. *Addictive Behaviors, 37*(8), 974-977. <https://doi.org/10.1016/j.addbeh.2012.03.015>
- Ward, K. P., Dennis, C. B., & Limb, G. E. (2018). The impact of stepfamily relationship quality on emerging adult non-medical use of prescription drugs. *American Journal of Drug and Alcohol Abuse, 44*(4), 463-471. <https://doi.org/10.1080/00952990.2017.1405010>
- Winward, J. L., Hanson, K. L., Tapert, S. F., & Brown, S. A. (2014). Heavy alcohol use, marijuana use, and concomitant use by adolescents are associated with unique and shared cognitive decrements. *Journal of the International Neuropsychological Society, 20*(8), 784-795. <https://doi.org/10.1017/S1355617714000666>
- Young, A. M., Glover, N., & Havens, J. R. (2012). Nonmedical use of prescription medications among adolescents in the United States: A systematic review. *Journal of Adolescent Health, 51*(1), 6-17. <https://doi.org/10.1016/j.jadohealth.2012.01.011>